Johnson & Johnson

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April 10, 2000

VIA FACSIMILE AND FEDERAL EXPRESS

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Docket No. 00D-0084; Draft Guidance for Industry on Special Protocol Assessment

Dear Sir or Madam:

Johnson & Johnson submits these comments on behalf of its affiliates, Janssen Research Foundation ("JRF") and R.W. Johnson Pharmaceutical Research Institute ("RWJPRI"), in response to the Food and Drug Administration's ("FDA") draft guidance for industry entitled "Special Protocol Assessment". In general, the draft guidance document is thoughtful, reasonable, and well written. JRF and RWJPRI appreciate the opportunity to comment and offer the following observations on the draft guidance:

I. General

We recommend that the guidance clarify the circumstances under which it would be inappropriate for FDA to review a protocol. In addition, we believe that if the agency decides to take a matter to an Advisory Committee, provisions should be in place to maintain strict confidentiality of the protocol.

II. Timing of Request

The requirement that a sponsor submit a protocol intended for special protocol assessment to FDA at least 90 days prior to anticipated commencement of the study appears excessive. The draft guidance provides that comments should be provided to the sponsor within 45 calendar days of receipt of the request for special protocol assessment (page 6, line

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177). It should not ordinarily take an additional 45 days to resolve any issues raised by FDA. Accordingly, a 90-day period would only be appropriate if the protocol were going to be reviewed by an Advisory Committee.

Moreover, the draft guidance assumes that an IND will be in place before a special protocol assessment is requested (see e.g., page 4, line 105). Such a requirement would penalize companies that perform Phase 1 and 2 studies outside the United States. Therefore, the guidance should provide that a special protocol assessment may occur even if an IND has not been filed with FDA.

III. Carcinogenicity Protocols

- The requirement of an additional 30-day notice period and submission of relevant background information before submitting a carcinogenicity protocol for review (page 3, lines 72-78) appears unnecessary and excessive. We recommend that this requirement be eliminated. Instead, we recommend that sponsors be required to submit all relevant background information related to design of the carcinogenicity study at the time of submission of the protocol.

- The draft guidance would prohibit a sponsor from receiving input on a protocol after the study has started (page 3, line 70). Given that carcinogenicity study designs can be modified in the early weeks of a two-year study with little impact on the outcome, eliminating the possibility of receiving input seems a harsh result in this context.

- Moreover, during the course of a two-year carcinogenicity study, designs are often modified based on new information. It is unclear, whether and how such study modifications are communicated to the agency.

IV. Stability Protocols

Most stability protocols are straightforward and those that are not can be reviewed in a shorter time frame than the proposed 45 days. We recommend that stability protocols be reviewed in a 30-day time frame instead.

V. Agency Assessment

- The draft guidance describes the review disciplines that will make recommendations to the division director on the appropriateness of a submission for special protocol assessment (page 6, line 160). We recommend that CDER include the statistical team leader in addition to the "clinical team leader, chemistry team leader, or pharmacology/toxicology team leader," as many of the issues will be statistical in nature. More importantly, however, we recommend that the agency describe the criteria by which it will decide whether a submission is appropriate for assessment.

- The draft guidance states that "if special protocol assessment is not appropriate . . . the division should notify the sponsor of the reasons for the determination as soon as possible after the Agency's receipt of the request." FDA should make and communicate to the sponsor this determination within a specified time frame, i.e., 10 days. This initial determination should not be resource intensive for the agency and the sponsor should be apprised of the decision in a timely manner.

- The draft guidance calls for a new 45-day clock when the sponsor changes the protocol during the initial review period in response to FDA comments provided before issuance of the special protocol assessment letter (page 6, line 181). The guidance should be changed to make clear that a protocol revision based on the agency's comments prior to the sponsor receiving a special protocol assessment letter does not start another 45-day clock. If the changes are made to incorporate FDA comments, the protocol should be reviewed under the original time frame allotted for discussion and resolution of protocol issues. It is understood, however, that a sponsor's response to FDA comments near the end of the 45-day review period, may make it impossible for the agency to meet its deadline to provide the assessment letter. In such cases, it is reasonable to allow for a two-week extension for the assessment letter if the revised protocol is submitted on or after day 30 of the 45-day clock, provided the revisions address FDA comments.

VI. Advisory Committee Review and Other Outside Review

We recommend that the guidance specify that the Advisory Committee Meeting will be a closed meeting and exempt from the open advisory committee disclosure guidance.

We are also concerned about the timeliness of Advisory Committee review and the fact that the sponsor has no apparent role in the decision as to whether Advisory Committee review is appropriate. While the PDUFA goal is a 45-day response time, the draft guidance describes a process with two separate 45-day periods plus an undetermined time period for the next scheduled Advisory Committee meeting. Moreover, the draft guidance does not ensure that the protocol will be reviewed at the next scheduled Advisory Committee meeting, but rather at the next *available* meeting. The meaning of "available" in this context is not clear; it may be later than the next scheduled meeting. Thus, the actual response time in cases where the agency opts for Advisory Committee review could be six months or longer, rather than the stated goal of 45 days. This uncertainty is particularly concerning given that the draft guidance provides the FDA complete discretion with regard to sending a protocol for outside review.

Under the process envisioned in the current draft, a sponsor could submit a protocol for special assessment and then be told 45 days later that it will be reviewed at a future Advisory Committee meeting. Forty-five days after the Advisory Committee meeting, the sponsor would receive the special protocol assessment letter from the FDA. We submit that neither 45-day period is justifiable. While it may reasonably take the agency 45 days to

review a protocol and respond with a letter, it should not take that long simply to decide to seek outside review. Nor should it take 45 days to send a letter to the sponsor after the outside review – by an Advisory Committee or other government consultant - has taken place.

We recommend instead that if FDA decides to request outside review of the protocol, that the agency discuss that decision with the sponsor within 30 days of the protocol having been submitted for special assessment. In that discussion, the agency should advise the sponsor of the date of the Advisory Committee meeting or the timing of the consultant review, as well as the reasons why the agency deems outside review necessary. The sponsor should then be given the opportunity to forego the special protocol assessment or accept the delayed assessment. Moreover, FDA should send the special protocol assessment letter within 15 days of the Advisory Committee meeting or consultant review.

VII. Changes in Documented Special Protocol Assessments

The "failure of a sponsor to follow a protocol that was agreed upon" (page 8, line 236) giving rise to voiding the agreements reached between the sponsor and FDA in the special protocol assessment, should be better defined so that immaterial protocol deviations are not triggering events. The guidance should distinguish between a systematic failure to conduct the study according to the agreed upon protocol and minor protocol deviations that often occur during the conduct of a study, even under the best circumstances.

Further, when the sponsor and FDA evaluate a change to a protocol (page 8, line 243), the prior agreement reached under the special protocol assessment should be considered when evaluating the proposed change. FDA should advise the sponsor whether or not the amendment will void the agreement so that the sponsor may decide on whether it is appropriate to proceed with the amendment.

* * *

We trust that these comments will be useful as the agency finalizes this important guidance document.

Respectfully submitted on behalf of

Janssen Research Foundation and
R.W. Johnson Pharmaceutical Research Institute,

Freddy A. Jiménez
Attorney at Law
Johnson & Johnson

** JOB STATUS REPORT **

AS OF APR 10 2000 11:24 AM PAGE. 01

J&J LAW DEPT

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DATE: April 10, 2000

TO: Dockets Management Branch (HFA-305)

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NUMBER OF PAGES INCLUDING THIS COVER SHEET: 5

COMMENTS: RE: Docket No. 00D-0084; Draft Guidance for Industry on Special Protocol Assessment

To Whom It May Concern:

Enclosed you will find a copy of a letter (which is being sent via Federal Express today) submitting comments on behalf of its affiliates Janssen Research Foundation and R.W. Johnson Pharmaceutical Research Institute in response to the above-mentioned subject.

Respectfully,

Freddy A. Jimenez, Esq.

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Eugene Swift – A 1996 Olympian representing the United Sta… …lympic Games in Sydney, Australia. He has worked at UPS for 14 years and is currently in the human resources department in Oakland, California. He is a member of the global UPS Athlete Training Assistance Program (ATAP), which provides employee-athletes with the support they need to pursue their Olympic dreams.